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Alcohol and Prostate Cancer in the NHANES I Epidemiologic Follow-Up Study

ROSALIND A. BRESLOW, PHD, MPH, LOUISE WIDEROFF, PHD, BARRY I. GRAUBARD, PHD, DIANE ERWIN, MA, MARSHA E. REICHMAN, PHD, REGINA G. ZIEGLER, PHD, MPH, AND RACHEL BALLARD-BARBASH, MD

PURPOSE: We prospectively investigated the association between alcohol consumption and prostate cancer in the Epidemiologic Followup Study (NHEFS) of the first National Health and Nutrition Examination Survey (NHANES I).

METHODS: There were two cohorts: 1) Cohort I, followed from baseline (1971–75) through 1992, included 5766 men ages 25–74 years (median follow-up = 17 years); and 2) Cohort II, followed from the first follow-up round for Cohort I (1982–84) through 1992, included the 3868 men in Cohort I free of prostate cancer in 1982–84 (median follow-up = 9 years). Alcohol consumption was assessed at baseline as usual consumption, and at follow-up as usual consumption and as distant past consumption at the ages of 25, 35, 45, and 55.

RESULTS: There were 252 incident cases of prostate cancer. Consistent with most previous studies, we found no significant associations between usual total alcohol consumption and prostate cancer in Cohorts I or II [p = non significant (NS)], except for a significant inverse association at the heaviest level of drinking in Cohort II [relative risk (RR) = 0.23, 95% confidence interval (CI) = 0.06–0.95]. Further study of heavy drinkers in Cohort II revealed significant inverse associations between distant past heavy drinking (defined as > 25 drinks/week) and prostate cancer at age 25 (RR = 0.20, 95% CI = 0.06–0.63), age 35 (RR = 0.30, 95% CI = 0.12–0.77), and age 45 (RR = 0.39, 95% CI = 0.17–0.93), but not at age 55 (RR = 0.43, 95% CI = 0.17–1.10).

CONCLUSIONS: These results suggest that it may be important to consider distant past alcohol consumption in etiologic studies of prostate cancer. However, our results were based on small numbers of cases who were heavy drinkers and require replication.

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KEY WORDS: Alcohol, Prostate Cancer, Cohort Study.

INTRODUCTION

Despite the fact that prostate cancer is one of the most common cancers among men in the United States (1), few risk factors are well-established other than age, race, and family history (2). Therefore, the identification of additional risk factors, particularly modifiable risk factors, is of considerable interest.

Although alcohol consumption has been proposed as a risk factor for prostate cancer incidence, most case-control studies (3–22), and cohort studies in general populations (21, 23–30) have not reported significant associations. There are exceptions. Two population-based cohort studies reported increased risk of prostate cancer among alcoholics; one by Tonnesen et al. in Denmark (31), and the other by Adami et al. in Sweden (32). A cohort study by Hirayama in Japan (33) also reported increased risk. Two case-control studies reported increased risk of prostate cancer in drinkers; one by De Stefani et al. in a study in Uruguay (34), and the other by Hayes et al. in a large, population-based study in the United States (35). A third case-control study by Jackson in Washington, D.C. (36) reported an inverse association.

The majority of studies on alcohol and prostate cancer have assessed usual alcohol consumption, generally over the previous year (21). Yet, clinical and epidemiologic evidence suggest that prostate carcinogenesis may span decades (37), implying the possible etiologic relevance of long-term alcohol consumption.

The purpose of this study was twofold: to examine the

From the Applied Research Branch, Division of Cancer Prevention and Control (R.A.B., R.B.-B.), Division of Cancer Epidemiology and Genetics (L.W., R.G.Z.), Biostatistics Branch, Division of Cancer Epidemiology and Genetics (B.I.G.), National Cancer Institute, Bethesda, MD; Information Management Services (D.E.) and R.O.W. Associates (M.E.R.), Rockville, MD.

Address reprint requests to: Dr. Rosalind Breslow, Centers for Disease Control and Prevention, 4770 Buford Hwy., MS K-55, Atlanta, Georgia 30341.

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Selected Abbreviations and Acronyms

NHANES I = First National Health and Nutrition Examination Survey of the United States
NHEFS = Nutrition and Health Examination Follow-Up Study
NCHS = National Center for Health Statistics

association between usual alcohol consumption and prostate cancer; and to examine the association between distant past alcohol consumption and prostate cancer. Prospective cohort data from 5766 male participants in the follow-up study of the first National Health and Nutrition Examination Survey of the United States (NHANES I), the Nutrition and Health Examination Follow-Up Study (NHEFS), were used to study these associations.

METHODS

Study Population

NHEFS Cohort. The NHEFS is a prospective cohort study arising from NHANES I, a nationally representative, cross-sectional, in-person interview and medical examination survey of the civilian non-institutionalized population of the United States, conducted between 1971 and 1975 by the National Center for Health Statistics (NCHS) (38). The NHEFS cohort includes all participants aged 25 through 75 years at the time of NHANES I (n = 14,407; male n = 5811); they have been periodically followed-up (median follow-up for men = 17.1 years) for vital and health status and re-interviewed. This study utilizes interview data from the NHEFS baseline (1971–75) and first follow-up (1982–84), and data on vital and health status collected in 1982–84, 1986, 1987, and 1992.

Information on the completeness of the NHEFS vital and health status follow-up has been presented in detail by Cox et al. (39). In brief, deaths were identified through the National Death Index. Data on health status during follow-up were obtained at interviews in which the participant or proxy was queried about physician diagnoses for medical conditions (including cancer) followed by requests for information on related overnight stays at health care facilities; the facilities were subsequently contacted to obtain relevant records. Data from the NHEFS are available on public use computer data tapes (NCHS, Hyattsville, MD).

Identification of Prostate Cancer Cases in the NHEFS Cohort. Of 5811 men in the baseline cohort, 299 men had ICD codes of 185 (invasive prostate cancer), 233.4 (prostate carcinoma in situ), v 10.46 (personal history of malignant prostate neoplasm), or 60.3–60.5 (prostatectomy surgical procedures) on the data tapes. R.A.B. and L.W. reviewed archived paper and/or microfiche records of interviews and overnight health care facility stays for each of these 299 men at NCHS in Hyattsville, MD resulting in reclassification of 34/299 as non-cases and exclusion of 11/299 as prevalent cases at baseline (299 − 34− 11 = 254). We classified the 254 remaining cases as definite (n = 168) or probable (n = 86) based on the type of confirmatory evidence available (none of the cases were *in situ*). Thus, among the 168 men classified as definite cases, the determination of 'definite' status was based on confirmation from histopathology reports in 152/168 and on confirmation from health care facility medical records in 16/168. Among the 86 men classified as probable cases, the determination was based on the availability of only interview data in 77/86 and only death certificates in 9/86.

Analytic Cohorts. We formed two separate cohorts, one originated in 1971–75; the other originated in 1982–84.

Cohort I (n = 5766; 252 cases, 5514 non-cases) originated in 1971–75 as follows: from the 5811 men (254 cases) in the NHEFS baseline cohort, we excluded an additional 2 cases and 32 non-cases without data on alcohol consumption.

Cohort II (n = 3775; 134 cases, 3641 non-cases) was the subset of Cohort I alive and free of prostate cancer at their 1982–84 interview who had data on alcohol consumption in 1982–84. It originated in 1982–84 and excluded (from the NHANES I original 5811 men) 2036 men as follows: 1202 deaths, 351 untraceable, 333 alive but not interviewed, 57 prevalent cases of prostate cancer (n = 11 prevalent at baseline + n = 46 prevalent by 1982–84), and 3 cases and 90 non-cases without data on alcohol consumption. The response rate for men at the 1982–84 interview was 88% [1 − (333 + 351/5811)].

Cohort IIa (n = 2070; 128 cases, 1942 non-cases) was a subset of Cohort II that excluded 1621 men younger than 56 years of age at their 1982–84 interview and another 84 lacking data on long-term drinking.

Assessment of Alcohol Consumption

Baseline. At baseline in 1971–75, the following questions were used to assess usual (previous year) alcohol consumption: "How often do you drink?", "Which do you most frequently drink—beer, wine, or liquor?" and, only for the most frequently consumed beverage, "When you drink (beer/wine/liquor) how much do you usually drink over 24 hours?". Because these questions resulted in the subject reporting the amount consumed *only for the most frequently consumed beverage*, potentially leading to under-reporting of alcohol consumption, we analyzed 1971–75 alcohol consumption data in two ways: frequency × amount (number of drinks per week) and frequency alone (number of days/week on which alcohol was consumed).

1982–84 Follow Up. At the 1982–84 follow up, usual alcohol consumption (previous year) was assessed using a semi-quantitative food frequency questionnaire which included the question: "On the average, how many (a) cans

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or bottles of beer; b) glasses of wine; c) shots or drinks of hard liquor, either straight or in a mixed drink) do you drink per day, week, month or year?"

Distant past alcohol consumption was assessed using the following questions: "Tell me the category which best describes your usual drinking pattern when you were about 25 years old." The question was repeated for ages 35, 45, and 55 and subsequent decades. The possible response categories were: 0, < 1, 1–9, 10–24, 25–39, 40–59, or 60+ drinks per week. Men drinking 25–39 drinks or more per week were defined as heavy drinkers. The lower bound of the 25–39 drinks per week category included men drinking approximately 3-1/2 drinks per day which is high according to 1995 US Dietary Guidelines for Americans (40). A summed score for drinking was created as follows: scores were assigned to each response category using the midpoint of each category, except for the open-ended highest category (60+ drinks per week), which was assigned a score of 70. Scores for each participant were summed over ages 25, 35, 45, and 55 (minimum summed score = 0; maximum summed score = 280). Quartiles of summed scores were analyzed using a quantile of non-drinkers at ages 25, 35, 45, and 55 as the referent.

Data Analysis

Associations between covariates and usual alcohol consumption were determined by chi-square tests of independence and analysis of variance. Relative hazards for prostate cancer among levels of usual and distant past alcohol consumption, adjusted for covariates described below, were estimated using Cox proportional hazard regression analysis. Estimated relative hazards from the Cox regressions are referred to as relative risks throughout this paper. For these analyses, the response was age to incidence of prostate cancer (41). Individuals who died during the follow-up without prostate cancer were censored at age of death. Individuals who survived the follow-up period and had no reported prostate cancer at their last follow-up interview were censored at age of last interview, which was the oldest age known to be prostate cancer-free. The baseline hazards in the Cox regressions were stratified by five-year intervals of age at baseline examinations in order to adjust for birth-cohort effects (41).

The NHEFS has a complex design that involves sample weighting, stratification, and clustering. To account for sample weights, design variables (i.e., variables used by NCHS to derive sample weights) were included as covariates in all regression analyses; these were: age (< 65 vs. ≥ 65 years), poverty census enumeration district (residence versus non-residence), family income (< $3000, $3000–6999, $7000–9999, $10,000–14,999, $15,000+), and race (black vs. non-black, Hispanics were included with whites) (42). Standard errors for the Cox regressions were computed in two ways: as design-based standard errors that take into account the stratification and cluster sampling of the complex sample design, and as model-based standard errors that assume the sample was a simple random sample (43). In general, design-based standard errors would be expected to be larger than model-based standard errors. However, the reverse was usually the case in this analysis, so we chose to be conservative and used the larger of the two standard errors for all statistical tests and confidence intervals.

Wald tests of simultaneous significance were used to determine whether the relative risks for categories of alcohol intake obtained from Cox regressions were simultaneously equal to one (44). The Wald test of simultaneous significance is analogous to testing overall statistical significance of factors with multiple levels in an analysis of variance. Statistical tests of trend for relative risk by increasing categories of alcohol intake were conducted by assigning each category a score (median intake in that category), including the assigned score in the Cox regression model as an independent variable, and using t-tests to determine the level of significance. We were concerned about the accuracy of the level of statistical significance obtained from Cox regressions for the distant past drinking at ages 25, 35, 45, and 55 in Cohort IIa because small numbers of cases were heavy drinkers. We therefore repeated these analyses using exact log-rank tests stratified by 5-year birth cohorts without including covariates (because numbers were too small in the highest categories of alcohol consumption) (41). The *p*-values from these analyses agreed with corresponding *p*-values previously obtained from Cox regression analyses.

All tests of significance were two-tailed with the level of significance set at 5%. Descriptive analyses were performed using SAS v 6.11 (SAS Institute, Cary, North Carolina). Cox regressions were performed using in-house software (41).

Cox regression analyses were performed using: 1) models which included only race and design variables as covariates; and 2) models which included race, education, region of the country, family history of prostate cancer, body mass index, physical activity level, and design variables.

RESULTS

Cohort I (1971–75)

About one-third of the men in Cohort I were non-drinkers (Table 1). Drinking decreased with age. Whites drank more than non-whites. There were more non-drinkers in the South than other regions of the country. Men with higher education drank more than those with lower education.

There was no association between usual alcohol consumption and prostate cancer (Table 2) whether drinks per week (frequency × amount) or frequency of drinking (days/week on which alcohol was consumed) were measured. For frequency of drinking relative risks (RRs) were 1.00, 1.04,

TABLE 1. Demographics of Cohort I (1971–75), expressed as percent distributions, according to level of alcohol consumption: NHANES I Epidemiologic Follow-up Study

Alcohol consumption categories (drinks/week)	Cohort I (N = 5766)[a]					
Median Drinks/week[b]	Non-drinker 0	>0–1 0.6	2–7 2.5	8–14 10	15–21 20	22+ 35
N	1768	793	1814	684	311	396
Age at baseline						
25–44	18.5	12.4	38.8	15.2	7.3	7.8
45–64	29.0	13.3	31.2	12.2	5.4	8.9
65+	46.1	15.8	23.5	7.8	3.2	3.7
Race						
White	29.7	13.7	31.7	12.3	5.6	6.9
Black	36.3	13.0	30.1	9.4	4.0	7.1
Other	29.4	24.7	32.9	8.2	3.5	1.2
Region						
Northeast	21.5	15.4	33.8	13.3	7.1	9.0
Midwest	25.8	12.5	33.1	14.0	6.1	8.6
South	46.2	12.5	25.4	9.1	3.0	3.9
West	27.3	14.8	34.0	11.6	5.7	6.5
Education						
<12	39.7	13.4	26.5	9.5	4.8	6.1
12	25.5	13.4	34.0	12.5	5.4	9.2
>12	18.8	14.8	38.3	15.6	6.5	6.0
Smoking						
Current	22.7	12.1	34.4	14.0	7.1	9.7
Former	34.6	14.0	30.1	11.3	4.5	5.6
Never	39.2	16.1	28.3	9.2	3.6	3.7

[a] p-values for chi square independence were <0.0001 for all variables except race (p = 0.0095).
[b] Usual drinking (past year).

1.00, 0.96, 1.13, 1.19, and 0.73 (respectively, never, 2–3 times/yr., 4–11 times/yr., 1–4 times/month, 2–3 times/week, about everyday, and everyday); all confidence intervals (CIs) included 1.00.

Cohort II (1982–84)

Demographic distributions were similar in Cohort II (data not shown). As shown in Table 2, there was a significant inverse association between alcohol consumption and prostate cancer at the highest level of total alcohol consumption (relative risk RR = 0.23, 95% CI = 0.06–0.95) but the Wald test of simultaneous significance was not significant. There was also a significant inverse association between the heaviest level of beer drinking and prostate cancer, but, again, the Wald test of simultaneous significance was not significant. There were no significant associations for wine or liquor.

We focused our examination of the association between distant past alcohol consumption and prostate cancer on heavy drinkers because of the suggestion of an effect in the analyses of usual drinking. As shown in Table 3, in 2070 men aged 55 years and older at first follow-up with complete information on alcohol consumption at the ages of 25, 35, 45, and 55 (Cohort IIa), we found significant inverse associations between heavy distant past consumption and prostate cancer at ages 25, 35, and 45, but not at age 55. The Wald tests of simultaneous significance for alcohol consumption were significant for ages 25, 35, and 45, but not 55.

The results presented in Tables 2 and 3 were not substantially changed by re-running our models as described below. Models using data collected in 1982–84 were re-run excluding men who, in their 1982–84 interview, stated they had stopped drinking because they were alcoholic/recovered alcoholic (n = 13 non-cases) or stated cirrhosis confirmed by a physician (n = 23 non-cases) or both (n = 35 non-cases). Models using data collected in both 1971–75 and 1982–84 were re-run defining only definite cases (n = 167) as cases; probable cases (n = 85) were grouped with the non-cases. Analyses using only definite cases as cases were not performed for the distant past drinking analyses at ages 25, 35, 45, and 55 due to small numbers. Models for alcohol consumption in 1971–75 and 1982–84 were re-run with a different referent group; i.e., non-drinkers were split into two categories, never drinkers and former drinkers. Models for beer, wine, and liquor consumption in 1982–84 were re-run using the same split categories as it was not possible to identify former consumers of specific beverages. Models for beer, wine, and liquor consumption in 1982–84 were adjusted for the consumption of each other beverage. Smoking status had been included in initial models and was dropped as it did not substantially alter results.

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TABLE 2. Risk estimates for usual alcohol consumption in Cohort I (1971–75) and Cohort II (1982–84): NHANES I Epidemiologic Follow-up Study[a]

	Cohort I 1971–75				Cohort II 1982–84				Cohort II 1982–84				Cohort II 1982–84			
	Total Alcohol				Total Alcohol				Beer				Wine			
	PY[b]	N Case	RR	95% CI	PY	N Case	RR	95% CI	PY	N Case	RR	95% CI	PY	N Case	RR	95% CI
Drinks/week																
Non-drinker	22,580	96	1.00		8,453	59	1.00		12,118	88	1.00		16,629	95	1.00	
>0–1	11,183	41	0.97	0.67 1.41	5,247	19	0.74	0.44 1.25	6,792	24	0.72	0.45 1.14	8,302	22	0.73	0.45 1.19
2–7	26,972	65	0.88	0.64 1.21	6,928	29	1.13	0.71 1.80	6,403	19	0.84	0.51 1.39	3,321	14	1.16	0.64 2.10
8–14	9,872	25	0.96	0.61 1.50	3,519	16	1.05	0.60 1.86								
15–21	4,365	8	0.85	0.41 1.75	1,834	9	1.12	0.55 2.30	3,492	4[c]	0.34	0.12 0.92	505	3	1.22	0.38 3.88
22+	5,192	17	1.42	0.84 2.40	2,707	2	0.23	0.06 0.95								

	Cohort II 1982–84				Cohort II 1982–84			
	Liquor							
	PY	N Case	RR	95% CI				
Drinks/week								
Non-drinker	14,354	82	1.00					
>0–1	7,839	26	0.96	0.61 1.50				
2–7	4,482	18	0.93	0.55 1.58				
8–14								
15–21	2,097	9	1.01	0.50 2.04				
22+								

[a] Cox regression models include race and design variables.
[b] PY = person years (years at risk for developing prostate cancer).
[c] The three highest categories of exposure for beer, wine, and liquor were combined into a single category of 8+ drinks per week due to small numbers of cases in each category.

TABLE 3. Risk estimates for distant past alcohol consumption at ages 25, 35, 45, and 55 in 2070 men aged 56 years and over (Cohort IIa) in 1982–84: NHANES I Epidemiologic Follow-up Study (NHEFS)[a]

	PY	Cases	RR	95% CI	
Distant past drinking[b]					
Non-drinker at age 25	4736	54	1.00		
Not heavy at age 25	7800	71	0.99	0.69	1.43
Heavy at age 25	1605	3	0.20	0.06	0.63
Non-drinker at age 35	4185	42	1.00		
Not heavy at age 35	8190	81	1.18	0.80	1.73
Heavy at age 35	1765	5	0.30	0.12	0.77
Non-drinker at age 45	4129	43	1.00		
Not heavy at age 45	8348	79	1.05	0.72	1.54
Heavy at age 45	1663	6	0.39	0.17	0.93
Non-drinker at age 55	4539	44	1.00		
Not heavy at age 55	8244	79	1.13	0.78	1.66
Heavy at age 55	1357	5	0.43	0.17	1.10
Summed score of distant past drinking (quartiles)[a,b]					
Non-drinker (score = 0)	3224	30	1.00		
Q1 (score = 0.5–10.0)	2711	28	1.27	0.75	2.16
Q2 (score = 10.5–20.0)	3455	37	1.37	0.83	2.24
Q3 (score = 22.0–67.0)	2141	17	1.12	0.61	2.07
Q4 (score = 68.0–280.0)	2610	16	0.81	0.44	1.49
p trend = 0.22.					

[a] Scores were based on drinks/week reported at ages 25, 35, 45, 55. Thus, the minimum summed score used to create quartiles was 0 and the maximum 280. Men drinking 25+ drinks/week (bold type below) were classified as heavy drinkers:

Drinks per week	Score
60+	**70**
40–59	**50**
25–39	**32**
10–24	17
1–9	5
<1	0.5
0	0

[b] Model = race + design variables.

DISCUSSION

We found no association between usual alcohol consumption and prostate cancer, confirming the results of most previous studies (21). However, we did find a significant inverse association between distant past alcohol consumption and prostate cancer. This finding is interesting, but should be interpreted cautiously. There were few heavy-drinking cases in our cohort and the biologic plausibility of the inverse association is not entirely clear.

The etiology of prostate cancer is poorly understood (37, 45, 46). Androgens, in particular the testosterone metabolite 5-α-dihydrotestosterone (DHT), appear to play a permissive though not inductive role in the development of prostate cancer (37). However, both laboratory and epidemiologic studies on the relationship between sex steroids and prostate cancer are inconclusive (45, 46).

The relationship between alcohol consumption and sex hormones in non-alcoholic men is likewise unclear. While acute alcohol consumption has been shown to decrease plasma androgens (47–51) and increase estrogens (47, 51, 52), the effects are not consistently reported, possibly due to methodological differences such as dose and elapsed time to measurement. In one study (49), testosterone levels raised by acute ingestion of alcohol subsequently returned to pre-ingestion values despite continued elevation in blood alcohol levels.

A relationship between alcohol consumption and sex hormones in alcoholic men could be postulated. Liver damage due to chronic alcohol abuse results in relative hyperestrogenism (46). Autopsy studies have shown a decreased incidence of prostate cancer in cirrhotics (53–55). It is interesting to note that no cirrhotic men in our study became cases and that while our cohort included a substantial number of heavy drinkers (n = 245 heavy drinkers at age 25), very few (n = 3 at age 25) became cases. We would also note that while we found no significant beverage-specific effects, heavy beer drinking tended to be inversely associated with prostate cancer. Beer, and wine to a lesser extent, may contain estrogenic substances (47).

Factors other than hormones might be hypothesized to mediate an association between alcohol and prostate cancer (56–58), but most would be expected to increase, not decrease, risk. For example, chronic alcohol consumption might increase or decrease risk by enhancing activation or deactivation of carcinogens or procarcinogens via induction of cytochrome P450 IIEI (56). Chronic alcohol consumption might increase risk through exposure of tissues to acetaldehyde, the carcinogenic primary metabolite of alcohol (58), or by decreasing immunity (57).

The major strengths of our study were that prostate cancer incidence over an approximately 17-year median follow-up was studied in regard to usual alcohol consumption at two points-in-time 10 years apart, and that data on distant past alcohol consumption were available. The availability of extensive data on alcohol consumption is a novel aspect of the NHEFS.

The major limitation of our study, common to most surveys of dietary intake, was the methodology for assessment of alcohol consumption. We studied both usual (previous year) and distant past alcohol consumption. Usual consumption in the 1971–75 NHEFS was likely under-reported due to incomplete questioning of participants. However, usual consumption in 1982–84 was assessed using a FFQ. FFQs have been shown to produce reasonably valid and reliable estimates of alcohol consumption by several investigators (59–63).

A more important dietary methodology issue for this study, given our finding of an inverse association between distant past alcohol consumption and prostate cancer, is the quality of the NHEFS data on distant past alcohol consumption. Liu et al. (64) studied this issue using data from the NHEFS. The correlation between distant past alcohol consumption recalled in 1982–84 for the decade 10 years before and consumption 10 years in the past as measured by self-reported usual consumption in 1971–75 was 0.7. Other studies have reported acceptable validity and reproducibility for distant past alcohol consumption recalled as far back as 30 years (59, 62, 65–67). However, it is possible that heavy drinkers might under-report. In the NHEFS study by Liu et al. (64), heavy drinkers tended to underestimate distant past alcohol consumption. Liu et al. defined heavy as $\geq$10 drinks per week while our study defined heavy as $\geq$25 drinks per week. Therefore, while misclassification of some heavy drinkers as less than heavy in our study is possible, we cannot determine the extent to which it might have occurred from the Liu et al. investigation. Some studies have found that heavy drinkers tend to over-report rather than under-report alcohol consumption (68, 69). Under-reporting, if it occurred in our study, would have biased results against finding the inverse association we found.

The other major limitation of our study was that few heavy drinkers developed prostate cancer. This limited the power of our analyses. In addition, we had no data on prostate cancer screening practices. We controlled for the marked increase in screening-related prostate cancers in the US between 1986 and 1991 (70) by using age-to-incidence as our response variable and by stratification on 5-year birth cohorts, but were unable to account for possible detection bias among heavy drinkers. Perhaps our results were affected by premature mortality among heavy drinkers; it was not possible to test this hypothesis. In addition, the possibility of residual confounding exists in any study of prostate cancer as few risk factors are known.

For usual drinking, our null findings are consistent with the majority of cohort and case control studies but do not agree with reports of significantly increased risk for prostate cancer in two Scandinavian alcoholic cohort studies (31, 32), a Japanese cohort study (33) and two case-control studies (34, 35). Regarding the cohort studies: our cohort consisted of a national sample of men that included heavy drinkers ($\geq$25 drinks per week). Drinkers at this level of intake are not necessarily diagnosed alcoholics. All of the participants in the Scandinavian studies were diagnosed alcoholics. Alcoholic populations may be exposed to different risks for prostate cancer than the general population. Possibly, protracted high alcohol exposure over decades, as captured in our study, at the level just below that resulting in cirrhosis, might be associated with different risk for prostate cancer than cirrhosis. The Japanese cohort study (33) was incompletely described, presenting only a point estimate of risk, making comparison with our study difficult. Regarding the case-control studies, recall and selection biases should be considered.

In conclusion, our finding of an association between

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distant past alcohol consumption and prostate cancer suggests that long-term consumption may be etiologically relevant. However, our results should be interpreted with caution as they were based on small numbers of cases who were heavy drinkers.

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